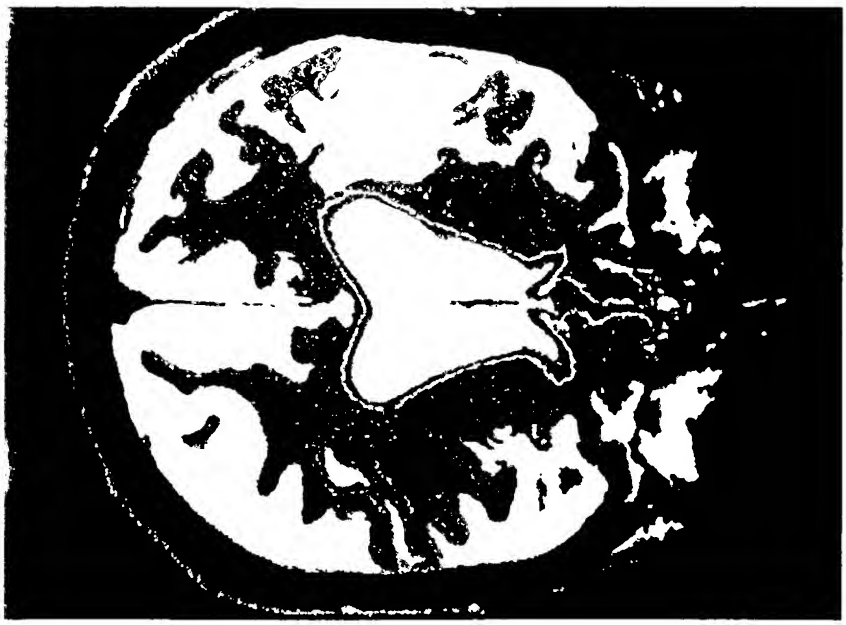
[illegible] While [illegible] these [illegible] occurs because the patient is developing dementia. There are reasons to believe that the actions of glutamate may be responsible, in part, for the loss of these cells. There are reasons to believe that blocking glutamate at the AMPA receptors may slow the progression of the dementia of PD. Memantine, an NMDA receptor blocking drug, improves behavior, memory and thinking in Alzheimer disease. It is possible that a drug such as **talampanel**, which blocks the AMPA receptors, may be more effective and may even slow the progression of Alzheimer disease.



Epilepsy and Brain Tumors

Glutamate is involved in triggering epileptic seizures. Drugs that block glutamate may be useful in treating epilepsy. A study under the sponsorship of the National Institutes of Neurological Disease and Stroke (Bethesda, Maryland) is under way looking at **talampanel** as a drug to treat epileptic seizures. Initial results are promising

Glutamate excites glial or support cells. These cells are also called astrocytes. The glial or support cells play a major role in nourishing nerve cells. The glial or support cells import nutrients from the bloodstream to the nerve cells and export waste products from the nerve cells to the spinal fluid. The common form of primary brain tumor is called an astrocytoma. A primary brain tumor is one that arises in the brain rather than a tumor that arises outside the brain and then secondarily seeds or metastasizes to the brain. A malignant astrocytoma is called a glioblastoma. This tumor kills 100 percent of patients within two years of diagnosis. It is thought glutamate may play a role in stimulating the growth of astrocytomas. A study under the sponsorship of the National Cancer Institute (Bethesda, Maryland) is underway looking at **talampanel** as a drug to treat astrocytomas.

Talampanel, Parkinson Disease, Dyskinesia

Inappropriate or uncontrolled excitation or stimulation with glutamate may be responsible, in part, for the progression of PD, for the progression of the dementia of PD, and for the occurrence of agitation, delusions and hallucinations (collectively called psychosis) in PD. Inappropriate or uncontrolled stimulation with glutamate may be responsible, in part, for the freezing phenomena that occur in PD. Inappropriate or uncontrolled stimulation with glutamate is probably responsible in large part for the dyskinesia of PD. Animal studies both in the United States and Europe have shown that **talampanel**, which blocks the actions of glutamate, can decrease or abolish levodopa-caused dyskinesia. A pilot study of 30 PD patients conducted in six United States Parkinson centers and a smaller study conducted in Europe indicate that **talampanel** may have a major role in decreasing or abolishing levodopa-caused dyskinesia. The Parkinson Center of the University of Miami Department of Neurology is now conducing a study on **talampanel** as a treatment for dyskinesia. To qualify for the study you must:

1. Have had PD for at least five years.
2. Have dyskinesia that are sufficiently disabling that you have considered DBS.

If you are interested in more information about the study, contact Dr. Lieberman at al@parkinson.org.

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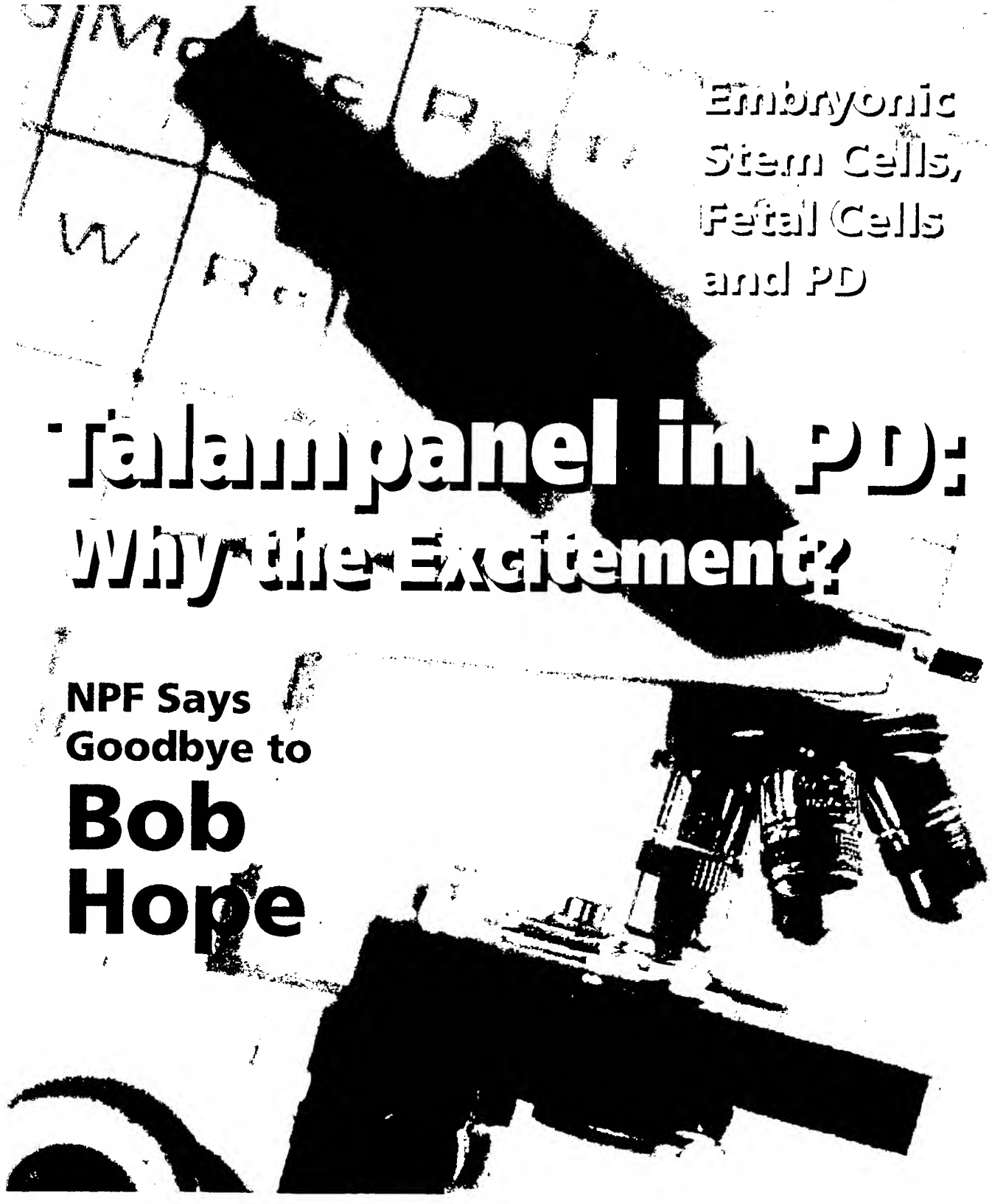
National Parkinson Foundation, Inc.



Embryonic Stem Cells, Fetal Cells and PD

Talampanel in PD: Why the Excitement?

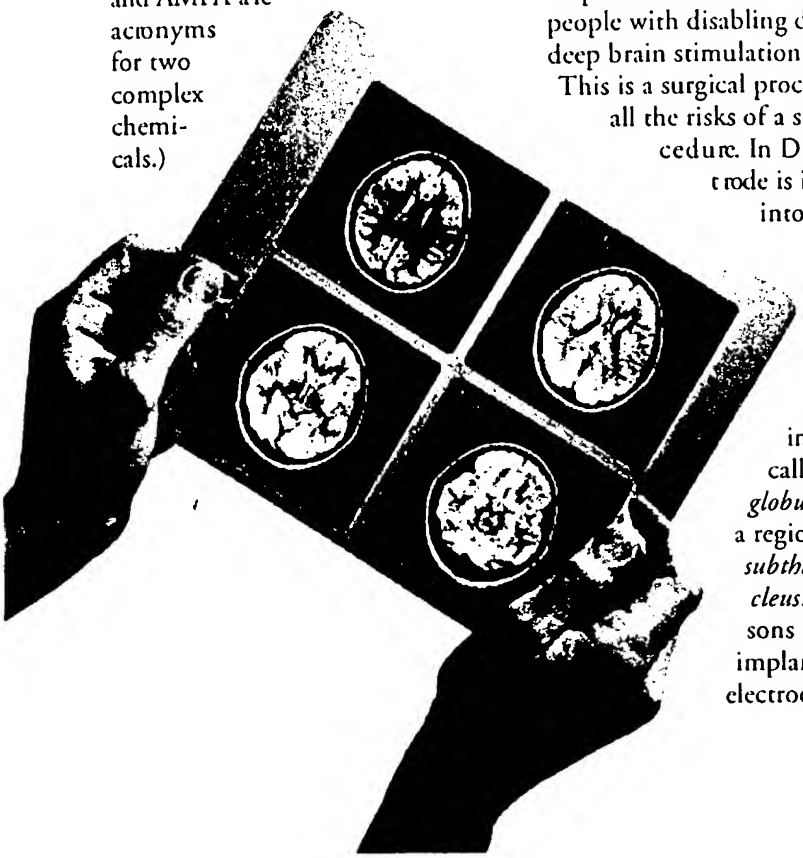
NPF Says Goodbye to Bob Hope

> "A pilot study of 30 PD patients in six United States Parkinson centers indicate that **talampanel** may have a major role in decreasing or abolishing levodopa-caused dyskinesia."

havior, some regulate memory, some regulate perception. Glutamate may be involved in all of these processes.

Glutamate Receptors: NMDA and AMPA

Glutamate from nerve cells in the cortex that regulate movement is transported to the putamen where it is released onto nerve cells in the putamen. The interaction takes place on a specialized part of the putamen nerve called the receptor. There are two receptors for glutamate. One receptor is called the NMDA receptor and the other is called the AMPA receptor. (NMDA and AMPA are acronyms for two complex chemicals.)



The AMPA receptor may be the more important of the two receptors. Until recently, there were only drugs that blocked the action of NMDA receptor, the less important receptor. Amantadine (Symmetrel), which can partially decrease or dampen dyskinesia, blocks the NMDA receptor. Memantine, a cousin of amantadine, which can partially improve thinking, behavior and memory in Alzheimer disease, blocks the NMDA receptor. **Talampanel** is the first drug that blocks the AMPA receptor to be used in people.

Deep Brain Stimulation

At present, the best treatment for people with disabling dyskinesia is deep brain stimulation (DBS). This is a surgical procedure, with all the risks of a surgical procedure. In DBS, an electrode is implanted into a region of the brain. The electrode may be implanted into a region called the *globus pallidus* or a region called the *subthalamic nucleus*. The reasons for implanting the electrode in one region over the other have not been defined. Most surgeons implant the electrode into the subthalamic nucleus, some implant it into the globus pallidus.

Nerve cells from the putamen, through glutamate and GABA, regulate nerve cells in the subthalamic nucleus and the globus pallidus. It is thought that glutamate is more important than GABA. DBS decreases or abolishes dyskinesia without slowing normal movement by restoring a balance between excitatory and inhibitory currents between the putamen, the subthalamic nucleus and the globus pallidus. Such a balance probably involves glutamate. It is possible that **talampanel**, a drug that blocks glutamate at the AMPA receptor, may be as effective as DBS in decreasing or abolishing dyskinesia.

Parkinson Dementia, Alzheimer Disease

The dementia of PD results from a loss of dopamine and other nerve cells outside the substantia nigra. Approximately 30 percent of all PD patients develop a dementia. The dementia usually appears after age 70. The initial symptoms of the dementia are agitation, delusions and hallucinations while the patient is on levodopa or a dopamine agonist. These symptoms markedly limit the use of levodopa and the agonists, and are usually the reason